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**Transposition of native chromatin for fast and sensitive epigenomic profiling of open chromatin, DNA-binding proteins and nucleosome position.**

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**Public Summary:**

We describe an assay for transposase-accessible chromatin using sequencing (ATAC-seq), based on direct in vitro transposition of sequencing adaptors into native chromatin, as a rapid and sensitive method for integrative epigenomic analysis. ATAC-seq captures open chromatin sites using a simple two-step protocol with 500-50,000 cells and reveals the interplay between genomic locations of open chromatin, DNA-binding proteins, individual nucleosomes and chromatin compaction at nucleotide resolution. We discovered classes of DNA-binding factors that strictly avoided, could tolerate or tended to overlap with nucleosomes. Using ATAC-seq maps of human CD4(+) T cells from a proband obtained on consecutive days, we demonstrated the feasibility of analyzing an individual's epigenome on a timescale compatible with clinical decision-making.

**Scientific Abstract:**

We describe an assay for transposase-accessible chromatin using sequencing (ATAC-seq), based on direct in vitro transposition of sequencing adaptors into native chromatin, as a rapid and sensitive method for integrative epigenomic analysis. ATAC-seq captures open chromatin sites using a simple two-step protocol with 500-50,000 cells and reveals the interplay between genomic locations of open chromatin, DNA-binding proteins, individual nucleosomes and chromatin compaction at nucleotide resolution. We discovered classes of DNA-binding factors that strictly avoided, could tolerate or tended to overlap with nucleosomes. Using ATAC-seq maps of human CD4(+) T cells from a proband obtained on consecutive days, we demonstrated the feasibility of analyzing an individual's epigenome on a timescale compatible with clinical decision-making.

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